

10/.527,799

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FILE COVERS 1907 - 14 Dec 2006 VOL 145 ISS 25

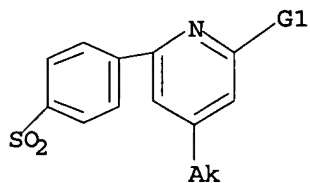
FILE LAST UPDATED: 13 Dec 2006 (20061213/ED)

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L1 STR



G1 O,N

Structure attributes must be viewed using STN Express query preparation.

L3 224 SEA FILE=REGISTRY SSS FUL L1

L4 3 SEA FILE=CAPLUS L3

=> d 14 1-3 ibib abs hitstr

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:471959 CAPLUS

DOCUMENT NUMBER: 143:1313

TITLE: Use of cyclooxygenase-2 selective inhibitors and combinations with neuroleptics for the treatment of schizophrenic disorders

INVENTOR(S): Hagan, James; Routledge, Carol

PATENT ASSIGNEE(S): Glaxo Group Limited, UK

SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005049034	A2	20050602	WO 2004-EP13076	20041117

WO 2005049034 A3 20050922

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1687001 A2 20060809 EP 2004-797978 20041117

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS

PRIORITY APPLN. INFO.:

GB 2003-26967 A 20031119
GB 2003-27937 A 20031202
WO 2004-EP13076 W 20041117

OTHER SOURCE(S): MARPAT 143:1313

AB The invention discloses the use of compds. which are cyclooxygenase-2 (COX-2) inhibitors, and pharmaceutically acceptable salts and solvates thereof, for the treatment of schizophrenic disorders. Schizophrenic disorders of the invention are to be intended schizophrenia, delusional disorders, affective disorders, autism or tic disorders, schizophreniform disorders, in particular chronic schizophrenic psychoses and schizoaffective psychoses, temporary acute psychotic disorders. Moreover, the invention discloses the use of a pyrimidine derivative known as a COX-2 inhibitor in combination with a neuroleptic drug for the treatment of schizophrenic disorders. Compound preparation is described.

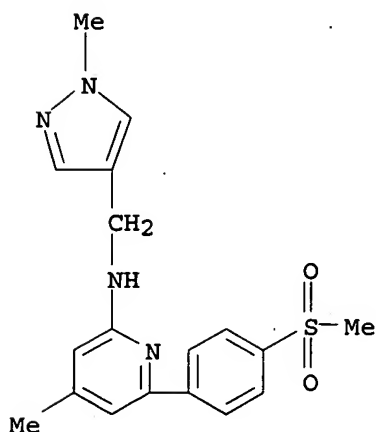
IT 675617-94-4P 675618-04-9P 675618-09-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(cyclooxygenase-2 inhibitors and combinations with neuroleptics for treatment of schizophrenic disorders)

RN 675617-94-4 CAPLUS

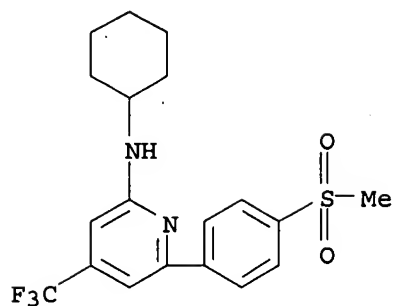
CN 2-Pyridinamine, 4-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



RN 675618-04-9 CAPLUS

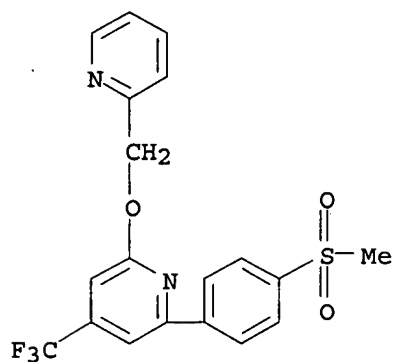
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RN 675618-09-4 CAPLUS

CN Pyridine, 2-[4-(methylsulfonyl)phenyl]-6-(2-pyridinylmethoxy)-4-(trifluoromethyl)- (9CI) (CA INDEX NAME)



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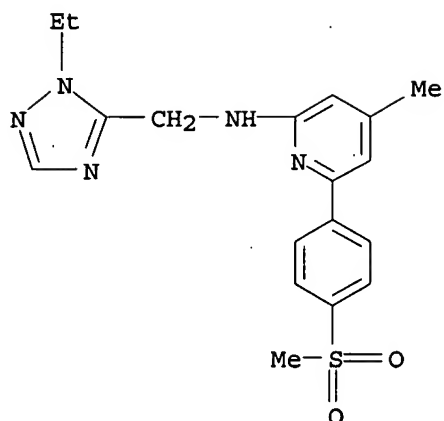
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cyclooxygenase-2 inhibitors and combinations with neuroleptics for treatment of schizophrenic disorders)

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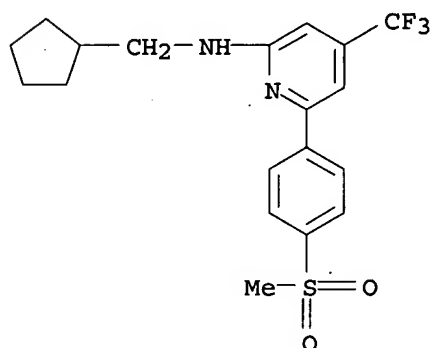
CN 2-Pyridinamine, N-[(1-ethyl-1H-1,2,4-triazol-5-yl)methyl]-4-methyl-6-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

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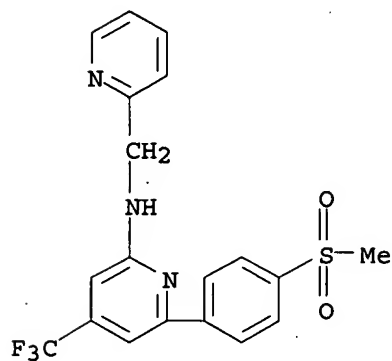
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CN 2-Pyridinamine, N-(cyclopentylmethyl)-6-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)- (9CI) (CA INDEX NAME)



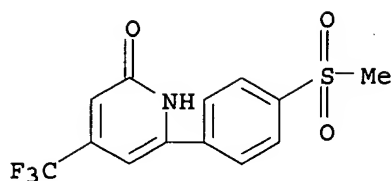
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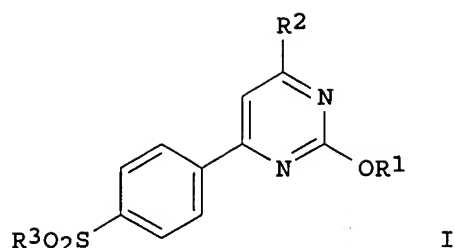
CN 3-Pyridinecarbonitrile, 4-ethyl-2-[(6-methyl-3-pyridinyl)methoxy]-6-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:471926 CAPLUS
 DOCUMENT NUMBER: 143:26625
 TITLE: Preparation of pyridines, pyrimidines, and
 pyrazolopyridazines as cyclooxygenase-2 inhibitors for
 the treatment of depressive disorders.
 INVENTOR(S): Hagan, James Joseph; Ratti, Emiliangelo; Routledge,
 Carol
 PATENT ASSIGNEE(S): Glaxo Group Limited, UK
 SOURCE: PCT Int. Appl., 56 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005048999	A2	20050602	WO 2004-EP13070	20041117
WO 2005048999	A3	20051103		
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EP 1687000	A2	20060809	EP 2004-797973	20041117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK, HR, IS				
PRIORITY APPLN. INFO.:			GB 2003-26967	A 20031119
			GB 2003-27937	A 20031202
			GB 2004-1862	A 20040128
			WO 2004-EP13070	W 20041117

OTHER SOURCE(S): MARPAT 143:26625
 GI



AB Use of title compds. e.g. [I; R1 = H, alkyl, fluoroalkyl, alkenyl, alkynyl, cycloalkylalkyl, bridged cycloalkyl, etc.; R2 = fluoroalkyl; R3 = alkyl, amino, carboxamide] for preparation of a medicament for treatment of depressive disorders is claimed. Thus, a mixture of 4-methylthioacetophenone and Me trifluoroacetate in MeOCMe3 was treated over 30 min. with NaOMe in MeOH followed by heating at 40° for ≥3 h. AcOH and S-Me 2-thiopseudourea were added followed by concentration and heating at 110° overnight. AcOH was added and the mixture was cooled to 50° followed by addition of aqueous Na tungstate and then 30% H2O2 over 3 h. followed by heating at 50° for ≥12 h. The mixture was cooled to 20° and aqueous Na sulfite was added over ≥30 min. followed by aging for 1 h to give 90% 2-methylsulfonyl-4-[4-(methylsulfonyl)phenyl]-6-trifluoromethylpyrimidine. The latter was heated overnight with K2CO3 in MeOH at 50° to give 88.4% 2-butoxy-4-[4-(methylsulfonyl)phenyl]-6-trifluoromethylpyrimidine (II). In the chronic inescapable shock in rats model, II at 10 mg/kg orally with paroxetine 5 mg/kg orally gave a full reversal of the chronic escape deficit.

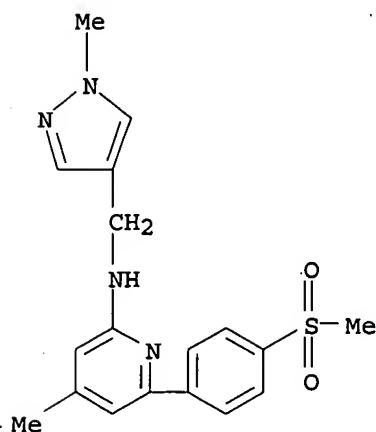
IT 675617-94-4P 675618-04-9P 675618-09-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of pyridines, pyrimidines, and pyrazolopyridazines as cyclooxygenase-2 inhibitors for the treatment of depressive disorders)

RN 675617-94-4 CAPLUS

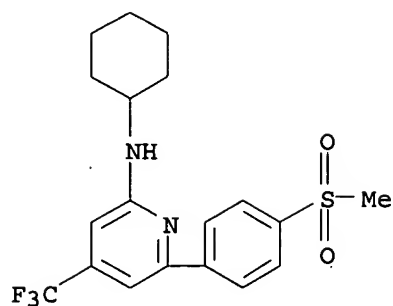
CN 2-Pyridinamine, 4-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



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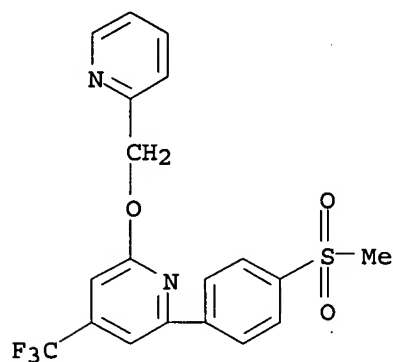
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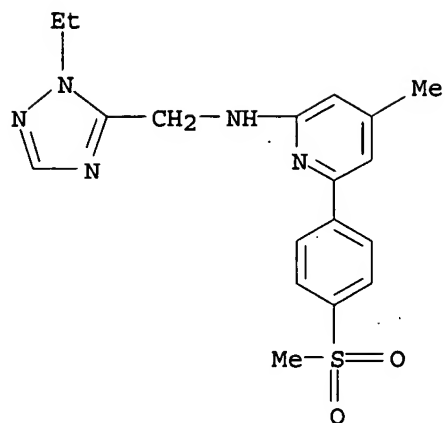
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of pyridines, pyrimidines, and pyrazolopyridazines as cyclooxygenase-2 inhibitors for the treatment of depressive disorders)

RN 675617-99-9 CAPLUS

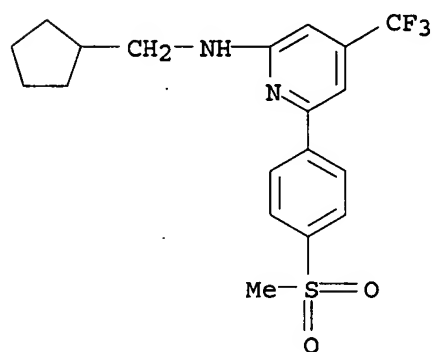
CN 2-Pyridinamine, N-[(1-ethyl-1H-1,2,4-triazol-5-yl)methyl]-4-methyl-6-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

10/.527,799



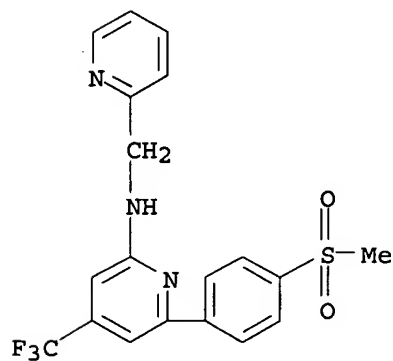
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CN 2-Pyridinamine, N-(cyclopentylmethyl)-6-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)- (9CI) (CA INDEX NAME)



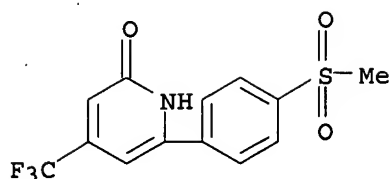
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CN 2-Pyridinemethanamine, N-[6-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



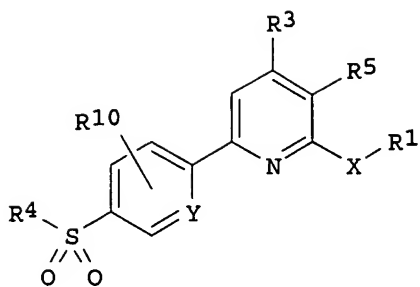
RN 675618-21-0 CAPLUS

CN 3-Pyridinecarbonitrile, 4-ethyl-2-[(6-methyl-3-pyridinyl)methoxy]-6-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

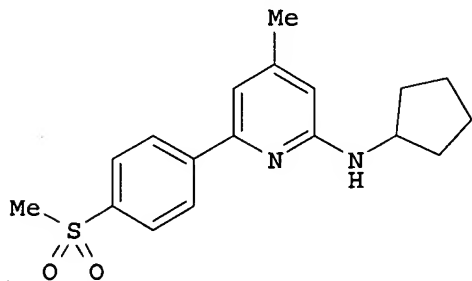


L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:252485 CAPLUS
 DOCUMENT NUMBER: 140:287274
 TITLE: Preparation of [(methylsulfonyl)phenyl]pyridines as COX-2 inhibitors
 INVENTOR(S): Beswick, Paul; Modi, Sandeep; Pegg, Neil; Skidmore, John; Swarbrick, Martin
 PATENT ASSIGNEE(S): Glaxo Group Limited, UK
 SOURCE: PCT Int. Appl., 79 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004024691	A1	20040325	WO 2003-EP11065	20030912
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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AU 2003276063	A1	20040430	AU 2003-276063	20030912
EP 1546107	A1	20050629	EP 2003-795019	20030912
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CN 1681788	A	20051012	CN 2003-821849	20030912
JP 2006507247	T2	20060302	JP 2004-535518	20030912
NO 2005000662	A	20050415	NO 2005-662	20050208
US 2006040988	A1	20060223	US 2005-527799	20050817
PRIORITY APPLN. INFO.:			GB 2002-21443	A 20020916
			WO 2003-EP11065	W 20030912
OTHER SOURCE(S):	MARPAT 140:287274			
GI				



I



II

AB Title compds. I [wherein X = O or NR₂; Y = CH or N; R₁ = H, (fluoro)alkyl, alkyloxyalkyl, alkenyl, alkynyl, cycloalkylalkyl, substituted cycloalkyl; R₂ = H, alkyl, or NR₁R₂ = (un)substituted heterocyclic ring; R₃ = (fluoro)alkyl; R₄ = alkyl, NH₂, amido; R₅ = H, (fluoro)alkyl, alkoxy carbonyl, halo, cyano, dialkylaminocarbonyl, alkylthio, alkylsulfonyl; R₁₀ = H, halogen; and pharmaceutically acceptable salts thereof] were prepared as cyclooxygenase 2 (COX-2) inhibitors. For example, substitution of 4-methyl-6-[4-(methylsulfonyl)phenyl]pyridin-2-yl trifluoromethanesulfonate with cyclopentylamine at 180°C for 14 h, gave II. I had IC₅₀ values for inhibition of COX-2 of 0.51 μM or less and at least a 100-fold selectivity for COX-2 over COX-1, based on comparison of the resp. IC₅₀ values. Thus, I and their pharmaceutical compns. are potent and selective inhibitors of COX-2 and useful for the treatment of COX-2 mediated conditions, such as inflammatory diseases.

IT 675617-88-6P 675617-89-7P 675617-93-3P
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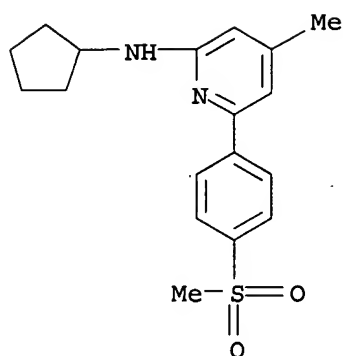
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)

(preparation of [(methylsulfonyl)phenyl]pyridines as COX-2 inhibitors)

RN 675617-88-6 CAPLUS

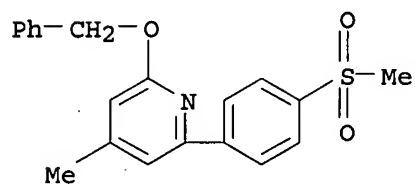
CN 2-Pyridinamine, N-cyclopentyl-4-methyl-6-[4-(methylsulfonyl)phenyl]- (9CI)
 (CA INDEX NAME)

10/.527,799



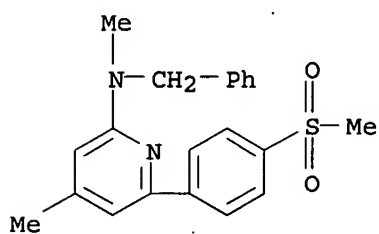
RN 675617-89-7 CAPLUS

CN Pyridine, 4-methyl-2-[4-(methylsulfonyl)phenyl]-6-(phenylmethoxy) - (9CI)
(CA INDEX NAME)



RN 675617-93-3 CAPLUS

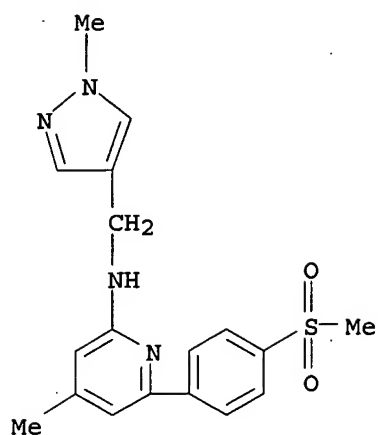
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RN 675617-94-4 CAPLUS

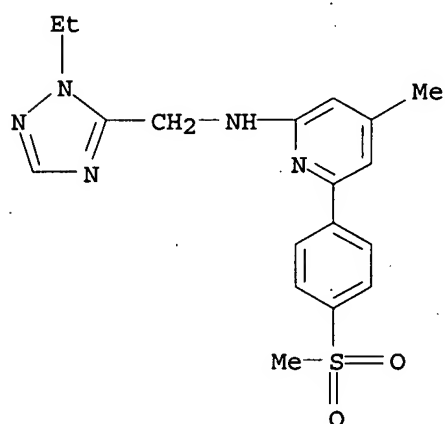
CN 2-Pyridinamine, 4-methyl-N-[(1-methyl-1H-pyrazol-4-yl)methyl]-6-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)

10/.527,799



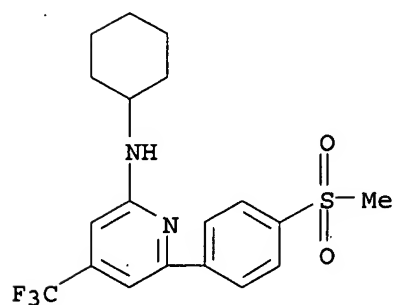
RN 675617-99-9 CAPLUS

CN 2-Pyridinamine, N-[(1-ethyl-1H-1,2,4-triazol-5-yl)methyl]-4-methyl-6-[4-(methylsulfonyl)phenyl]- (9CI) (CA INDEX NAME)



RN 675618-04-9 CAPLUS

CN 2-Pyridinamine, N-cyclohexyl-6-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)- (9CI) (CA INDEX NAME)



RN 675618-05-0 CAPLUS

CN 2-Pyridinamine, N-(cyclopentylmethyl)-6-[4-(methylsulfonyl)phenyl]-4-(trifluoromethyl)- (9CI) (CA INDEX NAME)